ABBOTT
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Division of Dockets Management (HFA-305)
The Food and Drug Administration
5630 Fishers Lane, room 1061,
Rockville, MD 20852

Re: **Docket No 2005D-0112. Draft Guidance for Industry on Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics.**

Abbott is pleased to have the opportunity to comment on the Draft Guidance on Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics, published in the Federal Register on April 04, 2005.

We commend FDA for their effort in providing guidance on clinical trial endpoints for cancer. The draft guidance provides an excellent review of clinical trial endpoints for the development of drugs and biologics for the treatment of cancer as well as useful insight into FDA's current thinking regarding the role of various endpoints to support approval. We have the following general comments for your consideration in finalizing this important guidance:

1. Survival is described as a gold standard endpoint in the development of oncology products. We encourage reconsideration of the emphasis on survival as a gold standard because of the same disadvantages cited in the draft guidance (*"...difficulties in performing studies large enough or long enough to detect a survival improvement, difficulties in determining a drug's effect on survival because of the confounding effects of subsequent cancer therapy, or a concern that the drug may be effective in only a small fraction of those treated, making it difficult to see an effect on survival in the whole population."*) Clearly, as an endpoint, survival, like other endpoints discussed in the guidance, is fraught with its own set of biases, complications, and practical considerations.

2. We agree with FDA and ODAC that progression-free survival (PFS) is generally a better surrogate endpoint for clinical benefit and for drug approval than time-to-progression (TTP).

3. Although the draft guidance includes discussion of endpoints involving symptom assessment (Section C, lines 430-506), we believe it could be improved by additional examples of well-executed symptom endpoints as a reference in future protocol development. This would be particularly useful with regard to the use of composite symptom endpoints as a measure of benefit such as fatigue, weight loss, and performance status, and others as appropriate.

4. The brief discussion of the role of biomarkers as endpoints in the development of oncology products (Section D, lines 508-528) provides three examples in which certain biomarkers are being considered as supportive evidence in clinical trials (paraprotein levels in myeloma, CA-125 in ovarian cancer, and PSA in prostate cancer). In addition to these examples, if there are other biomarkers that FDA is assessing in relation to additional forms of cancer, either as supportive or as primary endpoints, we recommend including a complete list in the guidance. Such a list would be a helpful guide in designing clinical trials and, in line with FDA's Critical Path efforts, may accelerate the identification of valid biomarkers for these conditions.

We thank the Agency for their consideration of our comments. Should you have any questions, please contact Ivone Takenaka, Ph.D., at (301) 255-0080 or by FAX at (301) 255-0090.

Sincerely,

D. L. Sporn

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